**EXAMINER'S AMENDMENT**

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization for this examiner's amendment was given in a telephone interview with Viola T. Kung, Ph.D. on December 15, 2008.

3. The application has been amended as follows:

In the claims:

Claims 1-32. (Canceled)

Claim 33. (Currently Amended) A method for detecting cervical dysplasia, cervical cancer or high grade cervical intraepithelial neoplasia in human cervical ~~body~~ samples comprising:

preparing a sample solution by solubilizing a human cervical sample in a lysis buffer;

determining the level of $p16^{INK4a}$ within the sample solution and comparing the determined level with the level of $p16^{INK4a}$ [[of]] in a normal human cervical sample;

determining the level of at least one normalization marker characteristic for the presence of ectocervical or endocervical cells within the sample solution, wherein said normalization marker is ~~a polypeptide comprising the amino acid sequence of~~ gamma-Catenin[[,]] comprising SEQ ID NO: 1; Ep-Cam[[,]]

comprising SEQ ID NO: 2; E-Cadherin[[,]] comprising SEQ ID NO: 3; alpha-1 Catenin[[,]] comprising SEQ ID NO: 4; alpha-2 Catenin[[,]] comprising SEQ ID NO: 5; beta-Catenin[[,]] comprising SEQ ID NO: 6; Involucrin[[,]] comprising SEQ ID NO: 7; or p120[[,]] comprising SEQ ID NO: 8;

determining a threshold value of the normalization marker by measuring the level of the normalization marker in a control sample solution containing an amount of ectocervical cells or endocervical cells;

comparing the level of the at least one normalization marker determined within the sample solution with the threshold value of the normalization marker; and

determining that said human cervical ~~body~~ sample contains cervical dysplastic cells, cervical cancer cells, or high grade cervical intraepithelial neoplastic cells[[,]] when the determined level of the at least one normalization marker in the sample solution is elevated above the threshold value[[,]] and the determined level of $p16^{INK4a}$ in the sample solution is elevated above the level of $p16^{INK4a}$ in the normal human cervical sample.

Claim 34 and 35. (Canceled)

Claim 36. (Original) The method according to Claim 33, wherein said method is used in early detection or primary screening tests of cervical lesions.

Claim 37. (Currently Amended) The method according to Claim 33, wherein said human cervical ~~body~~ sample is a swab, a secretion, an aspirate, a lavage, a cell, a tissue, a biopsy or a body fluid.

Claim 38. (Cancelled)

Claim 39. (Currently Amended) The method according to Claim 33, wherein said ~~amino acid sequence is~~ method comprises determining the level of Ep-Cam comprising SEQ ID NO: 2.

Claim 40. (Currently Amended) The method according to Claim 33, wherein said ~~amino acid sequence is~~ method comprises determining the level of at least one normalization marker selected from the group consisting of ~~SEQ ID NOs: 1, and 3-8~~ gamma-Catenin comprising SEQ ID NO: 1; E-Cadherin comprising SEQ ID NO: 3; alpha-1 Catenin comprising SEQ ID NO: 4; alpha-2 Catenin comprising SEQ ID NO: 5; beta-Catenin comprising SEQ ID NO: 6; Involucrin comprising SEQ ID NO: 7; and p120 comprising SEQ ID NO: 8.

Claims 41-54. (Cancelled)

Claim 55. (Currently Amended) The method according to Claim [[40]] 33, wherein said ~~amino acid sequence is~~ method comprises determining the level of gamma-Catenin comprising SEQ ID NO: 1.

Claim 56. (Currently Amended) A method for determining the presence of cervical dysplasia, cervical cancer or high grade cervical intraepithelial neoplasia in human cervical ~~body~~ samples comprising:

preparing a sample solution by solubilizing a human cervical sample in a lysis buffer;

determining the level of $p16^{INK4a}$ within the sample solution and comparing the determined level with the level of $p16^{INK4a}$ [[of]] in a normal human cervical sample;

determining the presence of at least one normalization marker characteristic for the presence of ectocervical or endocervical cells within the sample solution, wherein said normalization marker is ~~a polypeptide comprising the amino acid sequence of~~ gamma-Catenin[[,]] comprising SEQ ID NO: 1; Ep-

Cam[[,]] comprising SEQ ID NO: 2; E-Cadherin[[,]] comprising SEQ ID NO: 3; alpha-1 Catenin[[,]] comprising SEQ ID NO: 4; alpha-2 Catenin[[,]] comprising SEQ ID NO: 5; beta-Catenin[[,]] comprising SEQ ID NO: 6; Involucrin[[,]] comprising SEQ ID NO: 7; or p120[[,]] comprising SEQ ID NO: 8; and

determining that (i) said human cervical ~~body~~ sample contains cervical dysplastic cells, cervical cancer cells, or high grade cervical intraepithelial neoplastic cells[[,]] when at least one of said normalization markers is present in the sample solution[[,]] and the determined level of $p16^{INK4a}$ in the sample solution is elevated above the level of $p16^{INK4a}$ in the normal human cervical sample; or (ii) said human cervical body sample is inadequate for said determination of the presence of cervical dysplasia, cervical cancer or high grade cervical intraepithelial neoplasia[[,]] when none of said normalization markers is present within said sample solution.

Claim 57. (Previously Presented) The method according to Claim 56, wherein said method is used in early detection or primary screening tests of cervical lesions.

Claim 58. (Previously Presented) The method according to Claim 56, wherein said human cervical ~~body~~ sample is a swab, a secretion, an aspirate, a lavage, a cell, a tissue, a biopsy or a body fluid.

Claim 59. (Currently Amended) The method according to Claim 56, wherein said ~~amino acid sequence is~~ method comprises determining the level of Ep-Cam comprising SEQ ID NO: 2.

Claim 60. (Currently Amended) The method according to Claim 56, wherein said ~~amino acid sequence is~~ method comprises determining the level of at least one normalization marker selected from the group consisting of ~~SEQ ID NOs: 1, and 3-8~~ gamma-Catenin comprising SEQ ID NO: 1; E-Cadherin

comprising SEQ ID NO: 3; alpha-1 Catenin comprising SEQ ID NO: 4; alpha-2 Catenin comprising SEQ ID NO: 5; beta-Catenin comprising SEQ ID NO: 6; Involucrin comprising SEQ ID NO: 7; and p120 comprising SEQ ID NO: 8.

Claim 61. (Cancelled)

Claim 62. (Currently Amended) The method according to Claim [[60]] 56, wherein said ~~amino acid sequence is~~ method comprises determining the level of gamma-Catenin comprising SEQ ID NO: 1.

***Examiner's Statement of Reasons for Allowance***

4. The following is an examiner's statement of reasons for allowance:

Support for the amendment to the claims is found in the specification, including the claims, as originally filed.

$p16^{INK4a}$ is a cyclin dependent kinase inhibitor, which is ordinarily inactive or underexpressed in cancer cells; therefore, $p16^{INK4a}$ is generally thought of a tumor suppressor[1].

Thus, the overexpression of $p16^{INK4a}$ by the cervical cells of cervical dysplasia, cervical cancer, or high grade cervical intraepithelial neoplasms is an unexpected phenomenon, otherwise only taught or suggested by U.S. Patent No. 6,709,832-B1.

The claimed process is nevertheless an unobvious variant of the processes disclosed and claimed by U.S. Patent No. 6,709,832-B1, namely a method for detecting cervical carcinomas, cervical intraepithelial neoplasias, or cervical carcinomas *in situ* comprising determining the overexpression of cyclin-dependent kinase inhibitor p16 in a human cervical body sample by comparing the expression level of cyclin-dependent kinase inhibitor p16 within said sample to the expression level present in a healthy human cervical body sample, since

the prior art does not teach or fairly suggest modifying such a process to practice the claimed invention.

5. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

***Conclusion***

6. Claims 33, 36, 37, 39, 40, 55-60, and 62 have been allowed.

7. Claims 33, 36, 37, 39, 40, 55-60, and 62 have been as claims 1-12, respectively.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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[1] For a recent review of this topic, see, e.g., Liggett et al. (*J. Clin. Oncol.* 1998 Mar; 16 (3): 1197-1206).

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/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

slr
December 15, 2008